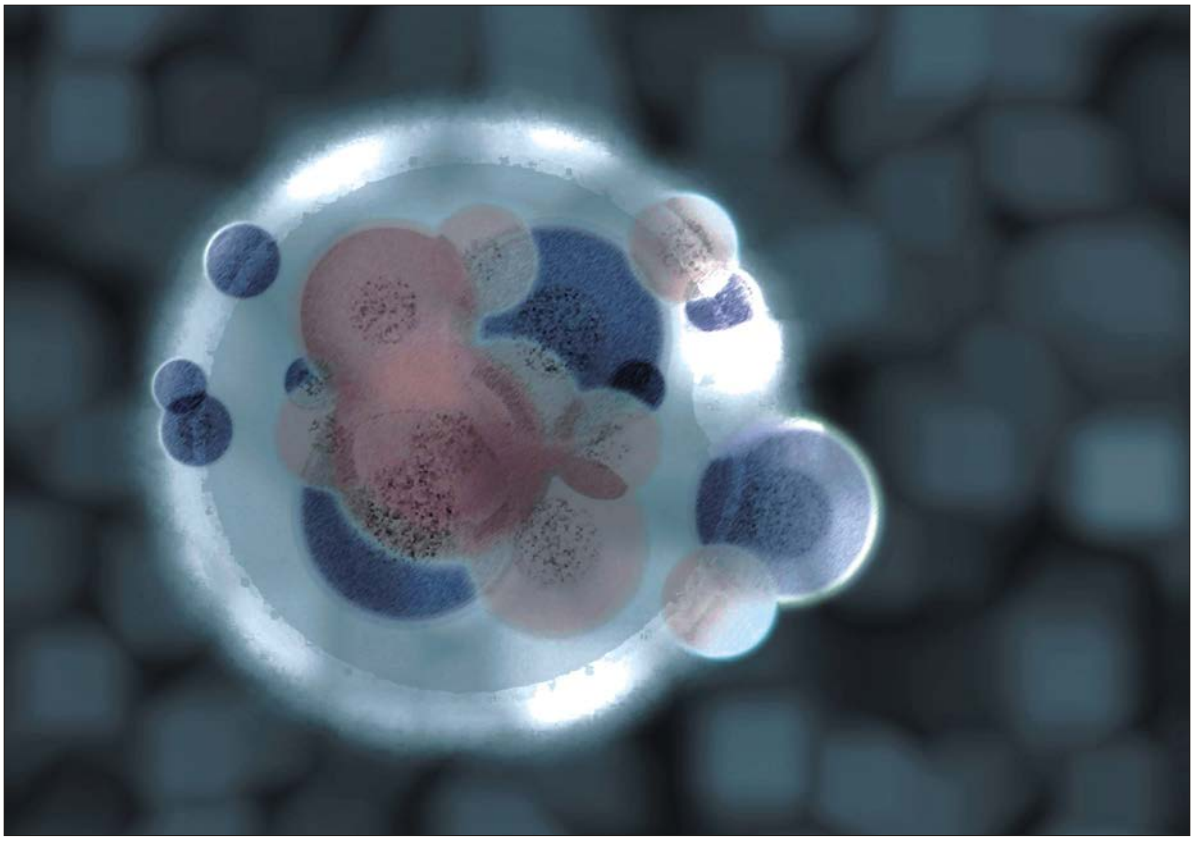

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Correlation of Serum Magnesium with Serum Parathormone in Regular Hemodialysis Patients

[1]Hamid Nasri, [1]Shahin Shirani M.D. and [2]Azar Baradaran
[1]Department of Internal Medicine, Hajar Medical, Educational and Therapeutic Center, Shahrekord University of Medical Sciences, Shahrekord, Iran
[2]Center of Research and Reference Laboratory of Iran, Department of Biochemistry, Hospital Bu Ali, Damavand st. P.O. Box 17115-365, 17117, Tehran, Iran

Abstract: To consider the relationship of serum magnesium with the activity of the parathyroid gland in maintenance hemodialysis patients we designed a study to investigate the role of serum magnesium in regulating the parathyroid secretion. The study was conducted on patients undergoing maintenance hemodialysis treatment. Predialysis serum calcium, phosphorus, magnesium, alkaline phosphatase, intact serum PTH (iPTH), serum 25-hydroxy vitamin D (25-OH Vit D) and plasma HCO_3^- were measured. The Urea Reduction Rate, duration and dosage of hemodialysis treatment were calculated also. In this study no significant correlation of serum magnesium with duration of hemodialysis treatment, alkaline phosphatase, plasma HCO_3^-, serum calcium and phosphorus patients were seen. In all patients a near significant inverse correlation of serum magnesium with iPTH ($r = -0.30$, $p = 0.079$) was found, also a significant positive correlation of serum magnesium with serum 25-hydroxy vitamin D levels ($r = 0.40$, $p = 0.009$) was seen. Earlier research concluded that some factors other than serum magnesium may be more important in the regulation of parahormone secretion in hemodialysis patients. A positive and strong association between serum magnesium with 25-hydroxy vitamin D level, needs to more attention to this aspect of hemodialysis patients.

Key words: Hemodialysis, serum magnesium, secondary hyperparathyroidism, parahormone, serum 25-hydroxy vitamin D level

INTRODUCTION

Secondary hyperparathyroidism (SHPT) is a common, important and treatable complication of end-stage renal disease (ESRD) (De Boer *et al*., 2002; Hörl, 2002; Moe and Drüeke, 2003). Hyperphosphatemia, hypocalcemia decreased expression of calcium and vitamin D receptors and parathyroid hormone resistance may be interact principally (Moe and Drüeke, 2003; Kates *et al*., 1997; Yamamoto *et al*., 1989; Portale *et al*., 1982; Gogusev *et al*., 1997; Korkor, 1987; Llach *et al*., 1975). The fact that many complications of secondary hyperparathyroidism are poorly reversible in the long-term (Nasri *et al*., 2004; Nasri Baradaran, 2004; Nasri, 2003; Nasri *et al*., 2003), emphasises the need for early management of secondary uremic hyperparathyroidism, starting with careful consideration of all the factors involved in the activity of the parathyroid glands of these patients (Hörl, 2002). In fact independent of the most important factors mentioned above which regulate parathyroid gland function, it has been believed that magnesium plays an important role in regulating the secretion of parathyroid hormone (PTH) (Cho *et al*., 2002). It is thought that magnesium may be able to modulate PTH secretion in a way similar to calcium (Guh *et al*., 2002). About the status of magnesium, it is found that as renal excretion is the major route of magnesium elimination from the body and as a positive magnesium balance would be expected under conditions of renal insufficiency (Mountokalakis, 1990) in chronic renal failure, the limited ability of the kidney to excrete an increased magnesium load may result in toxic concentrations of the ion in serum, while magnesium balance may be normal or even decreased in uremic patients. This is usually due to decreased dietary intake combined with the impaired intestinal magnesium absorption. Impairment of magnesium absorption seems

Corresponding Author: Hamid Nasri, Department of Internal Medicine, Hajar Medical, Educational and Therapeutic Center, Shahrekord University of Medical Sciences, Shahrekord, Iran
Tel: 0098 912 1439584 Fax: (00)98 381 2243715

to be related to deficient synthesis of the active metabolite of vitamin D by the non-functioning kidney (Mountokalakis, 1990). Following the institution of chronic hemodialysis treatment, the major determinant of magnesium balance is the concentration of magnesium in the dialysate. Thus in Chronic Renal Failure (CRF), nutritional intake, impaired absorption from the intestine, vomiting, diarrhea, the use of diuretics and acidosis may result in a negative balance and as mentioned accumulation of magnesium may be the consequence ofreduced renal excretion (Lindeman, 1986; Nasri and Baradaran, 2004). Magnesium concentrations are increased in serum and red cells in CRF patients. Bone concentrations and total body magnesium also appear to be increased (Nasri and Baradaran, 2004). Thus increased serum magnesium in hemodialysis patients may interact in parathyroid hormone secretion. In this regard studies showed that acute magnesium infusion decreases parathyroid hormone (PTH) secretion. However, the effect of chronic hypermagnesemia on PTH levels in dialysis patients is not well established (Navarro *et al*., 1999). Uncertainty about serum magnesium, Serum 25-hydroxy Vitamin D (25-OHVit D) levels and parathyroid hormone relationships in maintenance hemodialysis, specially about the relationship of 25-OH Vit D and serum magnesium because of very scares data sought us to design a study to investigate the association of serum magnesium with serum parathyroid hormone on a group of chronic hemodialysis patients containing diabetics and nondiabetic patients.

MATERIALS AND METHODS

This is a cross-sectional study that was conducted on patients with End-Stage Renal Disease (ESRD), undergoing maintenance hemodialysis (HD) treatment with acetate basis dialysate and polysulfone membranes. The study was carried out in March 2005 in the hemodialysis section of Hajar Medical Educational and Therapeutic Center of Shahrekord University of Medical Sciences in Shahrekord of Iran. According to the severity of the secondary hyperparathyroidism, each patient was under treatment for SHPTH with oral active vitamin D3 (Rocaltrol) and calcium carbonate and also Rena-Jel at various doses. According to the severity of anemia, patients were under IV iron therapy with Iron sucrose (venofer) at various doses after each dialysis session. All patients were under treatments of 6 mg folic acid daily, 500 mg L-Carnitine daily, oral Vitamin B-complex tablet daily and also 2000 U intravenous of Eprex (recombinant human erythropoietin (rHuEPO) for each patient after each dialysis session routinely. Exclusion criteria were active or chronic infection. For patients predialysis serum calcium (Ca), phosphorus (P), magnesium (Mg), alkaline phosphatase (ALP) were measured using standard kits. Intact serum PTH (iPTH) was measured by Radio Immuno Assay (RIA) method using DSL-8000 of USA. Serum 25-hydroxy Vitamin D3 (25-OHVit D) levels was measured by Enzyme-Linked Immunosorbent Assay (ELISA) method (normal range 25 to 125 nM L^{-1}) using Drug International (DRG) kits of Germany. Plasma HCO_3^- was measured by arterial blood gas. For the efficacy of hemodialysis the Urea Reduction Rate (URR) was calculated from pre- and post-blood urea nitrogen (BUN) data (Boag, 1994). Duration and doses of hemodialysis treatment were calculated from patients records. The duration of each hemodialysis session was four hours. For statistical analysis descriptive data are expressed as Mean±SD. Comparison between the groups was done using Student's t-test. Statistical correlations were assessed using partial correlation test. Statistical analysis were performed on total hemodialysis, females, males, diabetic and non diabetic populations separately. All statistical analysis were performed using the SPSS (version 11.5.00). Statistical significance was inferred at 5% level of significance.

RESULTS

The total patients were 41(F = 15, M = 26), consisting of 29 non diabetic hemodialysis patients (F = 11, M =18) and 12 diabetic hemodialysis patients (F = 4, M = 8). Table 1 shows that the Mean±SD of age of total patients were 46±17.6 years. The length of the time patients had been on hemodialysis were 29.5±34.7 months. The value of serum magnesium of total patients were 2.48±0.41 mg dL^{-1} and serum 25-hydroxy vitamin D levels of total patients were 7.60±9.45 nM L^{-1}. The value of serum iPTH of total patients was 408±440 pg mL^{-1}. In this study no significant deference of serum Mg, Ca, P, HCO_3^-, ALP, 25-hydroxy vitamin D levels between diabetics and nondiabetics were seen Significant deference of serum iPTH (r = 0.012) and URR (r = 0.046) between diabetic and nondiabetic patients were found. No significant differences of serum iPTH, Mg, Ca,P, plasma HCO_3^-, ALP and serum 25-hydroxy vitamin D levels and also duration of dialysis, dialysis dosage as well as age of the patients between males and females were seen. In this study no significant correlation of serum magnesium with variables consist of

Table 1: Mean±SD, Minimum and Maximum of age, duration and dosages of hemodialysis and also laboratory results of total, non-diabetic and diabetic hemodialyzed patients

Total patients (N = 41)		Minimum	Maximum	Mean±SD	Median
Age (years)		16	80	46±17.6	44
DH* (months)		2	156	29.5±34.7	18
Dialysis dose	sessions	18	1584	268±374	153
URR	(%)	39	76	58.7±8.75	58
HCO_3^-	(mEq L^{-1})	14	25	19.85±2.5	20
iPTH	(Pg m L^{-1})	16	1980	408±440	250
Ca	(mg dL^{-1})	5	10	7.7±0.99	8
P	(mg dL^{-1})	3	10	6.3±1.9	6.4
ALP	(IU L^{-1})	150	5487	632±878	428
Mg	(mg dL^{-1})	1.6	3.5	2.48±0.41	2.4
25-OHVit D (nM L^{-1})		0.30	36	7.6±9.4	3.2
Non diabetics n = 29		Minimum	Maximum	Mean±SD	Median
Age	(years)	16	80	43±17	41
DH*	(months)	2	156	35.5±40	20
Dialysis dose	sessions	18	1584	327±432	153
URR	(%)	50	76	60.6±7.78	60
HCO_3^-	(mEq L^{-1})	14	25	19.6±2.77	20
iPTH	(Pg mL^{-1})	22	1980	498±468	331
Ca	(mg dL^{-1})	6	10	7.8±0.88	8
P	(mg dL^{-1})	3.4	10	6.6±8	7
ALP	(IU L^{-1})	150	5487	764±1015	476
Mg	(mg dL^{-1})	1.6	3.3	2.49±0.4	2.4
25-OHVit D (nM L^{-1})		0.30	32	8.44±9.4	3.5
Diabetics n = 12		Minimum	Maximum	Mean±SD	Median
Age	(years)	27	79	55±17	57
DH*	(months)	6	24	15±6	15
Dialysis dose	sessions	54	216	127±54	132
URR	(%)	39	75	54±9.5	54
HCO_3^-	(mEq L^{-1})	18	25	20.33±1.77	20
iPTH	(Pg mL^{-1})	16	860	188±268	42
Ca	(mg dL^{-1})	5	10	7.5±1.2	7.5
P	(mg dL^{-1})	3	10	5.7±2	5.5
ALP	(IU L^{-1})	156	584	313±150	274
Mg	(mg dL^{-1})	2	3.5	2.4±0.4	2.3
25-OHVit D (nM L^{-1})		1.5	36	5.58±9.6	3.2

*Duration of hemodialysis treatment
**25-hydroxy Vitamin D

duration of hemodialysis, serum ALP, plasma HCO_3^-, serum Ca, P in total patients were seen. In total patients after adjusting for age, duration and dosage of dialysis, serum calcium, phosphorus and alkaline phosphatatase, a near significant inverse correlation of serum magnesium with serum iPTH (r = -0.30, p = 0.079, Fig. 1) was found. A significant positive correlation of serum magnesium with serum 25-hydroxy Vitamin D also remained strongly positive in nondiabetic, diabetic, female and male groups. A near positive levels (r= 0.40, p = 0.009, Fig.2) (adjusted for age) in total patients was seen. This significant association was of hemodialysis). In non-diabetic HD patients a near significant positive correlation of serum mg with

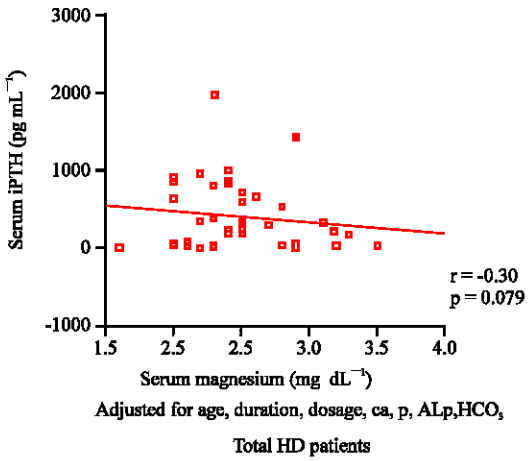

Fig. 1: Near significant inverse correlation of serum magnesium with iPTH

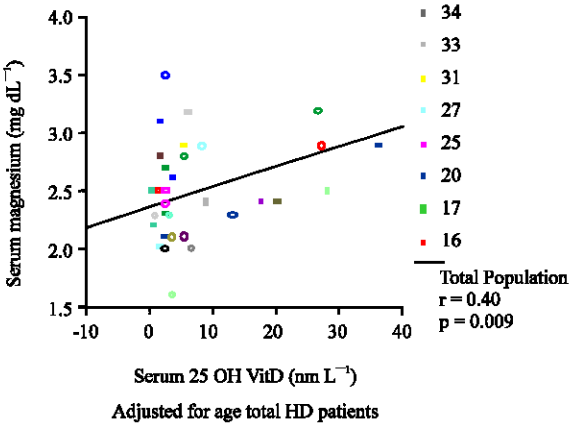

Fig. 2: Correlation of serum magnesium with 25 OH Vit D In total hemodialysis patients

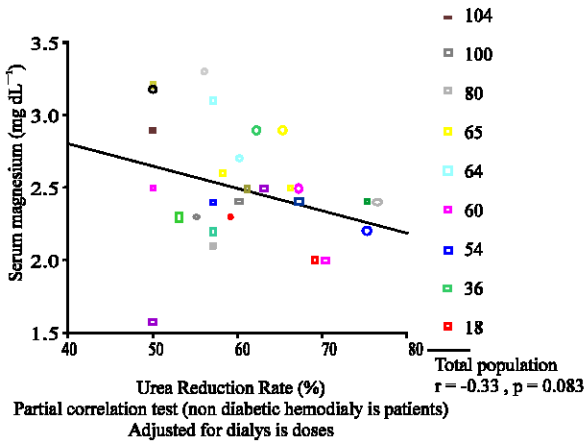

Fig. 3: Correlation of serum magnesium with dialysis adequacy by URR in non diabetic hemodialysis patients

plasma HCO_3^- (r= 0.33, p = 0.085) and a near significant and inverse correlation of serum Mg with dialysis adequacy (by URR) were seen (r = - 0.33, p = 0.083, Fig.3) correlation between serum mg and dialysis dosage was found (r = 0.27, p= 0.096) (adjustment for duration (adjusted for dialysis dosage for two above correlations).

DISCUSSION

In this study we found, no significant correlations of serum magnesium with duration of hemodialysis treatments, serum ALP, plasma HCO_3^-, serum Ca and P in total patients, a near significant inverse correlation of serum magnesium with iPTH and a significant positive correlation of serum magnesium with serum 25-hydroxy Vit D levels in total patients were found. Studies concerning the relationship of serum magnesium with serum parathormone revealved some interesting results. In the study conducted by Gohda *et al.* (2002) on eighty-six HD patients not treated with vitamin D, showed, serum intact PTH levels correlated negatively with serum magnesium and concluded that serum Mg level could predicted serum intact PTH levels. On the contrary to this study Gonella *et al.* (1981) on 22 uremic patients on chronic hemodialysis with different Mg concentrations in the dialysate, after 6-month period with differentiated Mg dialysis and significantly different Mg serum levels, no significant changes were observed in the PTH serum levels, they showed that PTH secretion in uremic patients on regular hemodialysis is not appreciably influenced by the Mg serum levels Navarro *et al.* (1999) in a study on 110 hemodialysis patients (mean age, 55±14 years; time on dialysis, 35±28 months) not receiving vitamin D, demonstrated that serum Mg was inversely correlated with PTH levels and PTH levels were predicted by Mg. They concluded that patients with inadequately low PTH levels showed greater serum Mg concentrations Serum Mg concentrations in dialysis patients are independently associated with PTH levels, suggesting that chronic hypermagnesemia may decrease PTH secretion and/or synthesis. In another study on 126 patients Guh *et al.* (2002) to consider pathogenesis of relative hypoparathyroidism (PTH< 200 pgm L^{-1}) in hemodialysis patients showed time-dependent PTH levels were inversely associated with serum magnesium level. McGonigle *et al.* (1984) to assess the influence of magnesium on circulating plasma iPTHin end-stage renal disease, on 20 patients receiving regular hemodialysis therapy who underwent plasma measurements of iPTH and 25-hydroxy Vit D levels before and 10 weeks after the magnesium concentration in the dialysate which was increased from 0.75 to 1.50 mM L^{-1}, showed a 36% rise in the mean predialysis plasma magnesium concentration and a 23% fall in the mean plasma iPTH concentration. Also mean plasma concentrations for 25-hydroxy Vit D levels also decreased, but this changes was not significant. McGonigle (1984) concluded that a rise in plasma magnesium concentration from elevated to significantly higher levels reduces circulating plasma iPTH in normocalcemic uremic patients with initially both normal and raised plasma PTH levels. In contrast to this study which implies an inverse correlation between serum Mg and 25-hydroxy Vit D levels, we found a strong positive correlation between serum magnesium and 25 OH Vit D levels. This significant association was also remained strongly positive in nondiabetic, diabetic, female and male groups. In conclusion, we found a near significant and inverse correlation of serum magnesium with serum parathormone. We concluded that some factors other than serum magnesium may be more important in the regulation of the parathormone secretion. We also showed a positive and strong association between serum magnesium with 25-hydroxy Vit D levels which is in contrast to the previous mentioned study. In hemodialysis patients, low serum 25OH Vit D levels could be a risk factor for secondary hyperparathyroidism needs to more notice to this aspect of hemodialysis patients.

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